

## **REMARKS**

This is a reply to the Office Action mailed March 28, 2003, with a shortened statutory response period of three (3) months from the mailing date, extended two months by Petition filed herewith. The Commissioner is hereby authorized to charge any additional fees to Deposit Account number 02-1818.

Claims 1-126 are presently pending in the application. Applicants have canceled claims 127 and 128 by this amendment.

### **I. Double Patenting Rejections**

Claims 1-128 have been provisionally rejected under 35 U.S.C. §101 and under the judicially created doctrine of obviousness-type double patenting. Claims 1-66 have been rejected in view of certain claims of another co-pending and commonly assigned application. Applicants submit that the amendment to claim 1 obviates this rejection for claims 1-60. Applicants further submit that these rejections can be more effectively addressed upon receiving a Notice of Allowance for claims in this or the other application that forms the basis of this rejection.

### **II. Rejections Under 35 U.S.C. §112**

Applicants have deleted the phrase “and other proteins” from claims 6, 21, 30, 35, 47, and 57, thereby obviating the rejection of these claims under 35 U.S.C. §112.

Applicants have amended claims 12 and 72 to recite “bile acid and a salt thereof” to correct a clerical-type error.

Applicants have amended claim 98 to clarify the language of section 98(iii).

Based upon these amendments, Applicants respectfully request a withdrawal of all rejections under 35 U.S.C. §112.

### **III. Rejections under 35 U.S.C. §102**

Claims 1-5, 10, 11, 17-20, 25-29, 31-34, and 39 stand rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 5,133,908. Applicants respectfully traverse these rejections.

The ‘908 Patent discloses a method for preparing a dispersible colloidal system of spherical particles having a size less than 500 nm. The method includes the steps of:

- 1) preparing a liquid phase of a substance in a solvent and a surfactant;
- 2) preparing a liquid phase of a non-solvent, the non-solvent being miscible in all proportions with the solvent;
- 3) the addition of the solutions of 1) and 2) with the other with moderate stirring to produce a colloidal suspension of nanoparticles; and
- 4) optionally removal of solvents.

Claim 1 recites a method for preparing crystalline particles. There is no disclosure in the '908 Patent for "adding energy to the pre-suspension" or for preparing crystalline particles. Therefore, the rejection of claims 1-5, 10, 11, 17-20, 25-29, 31-34, and 39 is improper under 35 U.S.C. §102.

#### **IV. Rejections Under 35 U.S.C. §103**

The Examiner has rejected claims 1-5, 7-20, 22-29, 31-34, 36-46, 48-56, 58, 59, and 66-97 under 35 USC 103(a) in view of the '908 patent discussed above. Applicants respectfully traverse this rejection.

The '908 patent does not recite an energy adding step as recited in all claims pending in this application. Indeed, the '908 patent teaches away from utilizing an energy adding step by disclosing as follows:

"...and the use of sophisticated equipment with high energy requirements (sonicators, homogenizers...) constitute serious handicaps to their industrial application." (Col. 1, 57-59).

"Since this emulsion must be very fine, the use of surfactants and the necessary equipment (sonicator, etc.) is essential for the production of nanoparticles of appropriate size." (Col. 2, lines 4-6)

Stainmesse specifies that it is an advantage of its method not to require the supply of energy: "The process for the preparation of nanoparticles according to the invention offers the following advantages compared with known processes: the production of nanoparticles smaller than 500 nm and in particular of about 200 nm by means of a simple method not requiring the supply of energy." (Col., 4, lines 61-66)

Accordingly, the Examiner has failed to present a prima facie case of obviousness.

Further, the '908 Patent teaches away from making crystalline particles, as recited in claims 1-59. The '908 Patent discloses in Example 14 that the disclosed process when carried out using indomethacin yields non-crystalline particles (Col. 8, lines 65-67).

Further, the '908 Patent teaches away from the methods recited in claims 60-65. Claim 60 recites a method for making submicron sized particles including the step of annealing a pre-suspension. The term "annealing" is defined as "...the process of converting matter that is thermodynamically unstable into a more stable form by single or repeated application of energy (direct heat or mechanical stress), followed by thermal relaxation." (specification, pg. 7, lines 3-5.) The '908 Patent discloses, as set forth above, that is process does not require the addition of energy, and, therefore, teaches away from an annealing step.

Further, the '908 Patent makes no mention of preparing friable particles as recited in claims 66-97.

The Examiner has rejected claims 60-65 and 98-128 under 35 U.S.C. §103 in view of the combination of the '908 Patent and U.S. Patent No. 6,063,138 (*Hanna*). Because the '908 Patent teaches away from annealing particles, as is required of claims 60-65, the '908 Patent cannot be combined with *Hanna*.

Claims 98-126 recite a method for making sub-micron sized particles including the step of seeding. Because the '908 Patent appears to disclose a process for forming amorphous particles, there would no reason to utilize a seeding step of *Hanna*. *Hanna* discloses that seeding causes "nucleation and the formation of embryos or nucleation sites, which can act a centers of crystallization for the substance of interest." (Col. 11, lines 5-16). Accordingly, seeding appears to be antithetical to the methods of the '908 Patent, and, therefore, these references are not properly combinable.

Accordingly, Applicants respectfully submit the pending claims are non-obvious, and patentable in view of the '908 Patent or the '908 Patent and *Hanna*.

In view of the foregoing Amendments and Remarks, Applicants respectfully submit that Claims 1-126 are in condition for allowance and respectfully request early notice of the same.

Respectfully submitted,

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